L Number	Hits	Search Text	DB	Time stamp
1	4642	(retrovirus retroviral lentiviral lentivirus) SAME (packaging producer)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/17 14:36
19	1183	((retrovirus retroviral lentiviral lentivirus) SAME (packaging producer)) and transplant	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/17 14:37
25	10	"6540995" "6207455"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/17 14:47
31	2	"6303380"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/17 14:40
37	38	"5529774"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/17 14:40
43	58	kingsman WITH alan	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/17 14:48
55	17	(kingsman WITH alan) and (producer packaging)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/17 14:49

L5 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2003 ACS
AN 1997:650467 CAPLUS
DN 127:315589
TI Cytochrome P450 encoding **retroviral** vectors and their use as antitumor agents
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
IN Gunzburg, Walter H.; Karle, Peter; Saller, Robert Michael
AB A replication-defective **retroviral** vector carrying a cytochrome P 450 gene under transcriptional control of target cell specific regulatory elements or promoters, or X-ray inducible promoters is disclosed.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9735994	A2	19971002	WO 1997-EP1585	19970327
WO 9735994	A3	19971120		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2250173	AA	19971002	CA 1997-2250173	19970327
AU 9723827	A1	19971017	AU 1997-23827	19970327
AU 713382	B2	19991202		
EP 892852	A2	19990127	EP 1997-919307	19970327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 331765	A	20000228	NZ 1997-331765	19970327
JP 2000509249	T2	20000725	JP 1997-534051	19970327
CZ 288074	B6	20010411	CZ 1998-3050	19970327
RU 2185821	C2	20020727	RU 1998-119459	19970327
NO 9804540	A	19980928	NO 1998-4540	19980928
US 6540995	B1	20030401	US 1999-442979	19991118

L5 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2003 ACS
AN 2000:15346 CAPLUS
DN 132:89228
TI Lentiviral vectors for **packaging** and transduction in gene therapy
SO PCT Int. Appl., 311 pp.
CODEN: PIXXD2
IN Chang, Lung-Ji
AB **Packaging** vectors comprising a nucleotide sequence encoding Gag and Pol proteins of a ref. lentivirus are provided. The **packaging** vectors differ from ref. lentiviruses at least in that: (a) its major splice donor site is either deleted, or if provided, while functional, differs in sequence from that of said ref. lentivirus sufficiently so that said major splice donor site is not a potential site for homologous recombination between said **packaging** vector and said ref. lentivirus; and (b) it lacks a functional major **packaging** signal. After introduction into a suitable host cell, the vector is capable of causing such cell, either through expression from said vector alone, or through co-expression from said vector and a second vector providing for expression of a compatible envelope protein, to produce **packaging** vector particles comprising functional Gag and Pol proteins and having a normal or a pseudotyped envelope. The particles are free of the RNA form of said **packaging** vector as a result of (b) above, where said cell, as a result of said expression or co-expression, produces particles **encapsulating** the RNA form of a transducing [illegible] **packaging** [illegible]

[illegible] **packaging** [illegible]

studied using different human cell types including TE671 muscle, 293 kidney, HepG2 liver, neuronal stem cells and primary CD34+ hematopoietic progenitor cells, and nonhuman primary rat neural and muscle cells. Transduction efficiency was assayed over short and long duration

L9 ANSWER 3 OF 256 CAPLUS COPYRIGHT 2003 ACS
AN 1993:185111 CAPLUS
DN 118:185111
TI In vivo gene transfer using implanted **retroviral** **producer** cells for killing of tumor cells
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
IN Barba, David; Gage, Fred H.
AB A method of transferring a therapeutic gene or genes into dividing mammalian tumor cells in order to kill them is described. **Producer** cells contg. proviral DNA and producing a defective **retrovirus** contg. a therapeutic gene in place of a **retroviral** gene required for replication are prepd. These cells are grafted in proximity to the dividing tumor cells in order to infect the tumor cells with the modified **retrovirus**. The tumor cells are then killed by administering a substance that is activated by the product of the therapeutic gene to give a metabolite that kills the tumor cells. Cells producing defective Moloney murine leukemia virus expressing the gene for .beta.-galactosidase were produced. These cells were injected into the tumors of rats having intracranial C6 tumors. .beta.-Galactosidase activity was found in the tumor cells. An in vitro expt. using cells producing virus expressing the herpes simplex thymidine kinase gene was described. The expt. demonstrated transfer of the gene to C6 glioma cells and killing of these cells with acyclovir

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9304167	A1	19930304	WO 1992-US6790	19920812
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
US 5529774	A	19960625	US 1991-744335	19910813
EP 602118	A1	19940622	EP 1992-918569	19920812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
JP 06509943	T2	19941110	JP 1992-504427	19920812

L9 ANSWER 7 OF 256 CAPLUS COPYRIGHT 2003 ACS
AN 1986:220146 CAPLUS
DN 104:220146
TI **Retroviral** gene transfer vectors
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
IN Verma, Inder Mohan; Miller, Arthur Gene; Evans, Ronald Mark
AB **Retroviral** gene vectors such as pSAM are constructed for the cloning of eukaryotic cDNA sequences in human and (or) murine cells. The recombinant DNA mols. contained in the vectors contain a genome **packaging** sequence, a promoter sequence for transcription initiation such as a viral 5' long terminal DNA repeat region (LTR), a 3'-**retroviral** LTR contg. a genome insertion site, a eukaryotic cDNA sequence, and a truncated viral coat protein gene. The coat protein gene mutation renders the DNA mol. incapable by itself of **packaging** its genome as a **retrovirus**. The **retroviral** genomes contg. the recombinant DNA mols. are rescued as complete **packaging** virions by amphotropic replication-competent helper virus vectors (eg. Moloney murine leukemia virus) which contain the coat protein gene. Host cells infected with the recombinant **retrovirions** are **transplantable** into host animals where the cloned gene product is expressed. The application of **retrovirus** vectors to the mol. cloning of the human gene for hypoxanthine phosphoribosyltransferase and the rat growth hormone gene is discussed. These **retrovirus** vectors may be useful in correcting genetic deficiencies such as that found in humans with Lesch-Nyhan syndrome.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 8600922	A1	19860213	WO 1985-US1442	19850729
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
EP 192658	A1	19860903	EP 1985-903951	19850729
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				

```
> d his

     (FILE 'HOME' ENTERED AT 12:58:40 ON 17 JUN 2003)

     FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
     AT 12:59:27 ON 17 JUN 2003
L1        103059 S RETROVIR?
L2          5519 S L1 AND (PACKAG? OR PRODUCER?)
L3            45 S L2 AND ENCAPSUL?
L4            27 DUP REM L3 (18 DUPLICATES REMOVED)
L5            27 FOCUS L4 1-
L6             0 S L2 AND TANSPLANT?
L7           534 S L2 AND TRANSPLANT?
L8           256 DUP REM L7 (278 DUPLICATES REMOVED)
L9           256 FOCUS L8 1-
L10           17 S L9 AND (EX VIVO)
L11           17 SORT L10 PY

=>
```

in tissue culture. The safety, expression kinetics, duration, and integration status of various lentiviral HP/TV vector systems are presented.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000000600	A2	20000106	WO 1999-US11516	19990526
	WO 2000000600	A3	20001012		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6207455	B1	20010327	US 1997-935312	19970922
	CA 2333481	AA	20000106	CA 1999-2333481	19990526
	AU 9943126	A1	20000117	AU 1999-43126	19990526
	EP 1082447	A2	20010314	EP 1999-957641	19990526
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

L5 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2003 ACS
AN 1997:783792 CAPLUS
DN 128:53291
TI Device and method for **encapsulated** gene therapy in the central nervous system
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
IN Hammang, Joseph P.; Aebischer, Patrick
AB Methods and devices are provided for gene therapy using **encapsulated packaging** cell lines to deliver viral particles carrying at least one heterologous gene encoding at least one biol. active mol.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9744065	A2	19971127	WO 1997-US8463	19970520
WO 9744065	A3	19971224		
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6027721	A	20000222	US 1996-650726	19960520
AU 9731317	A1	19971209	AU 1997-31317	19970520
AU 708173	B2	19990729		
EP 906124	A2	19990407	EP 1997-926594	19970520
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000512271	T2	20000919	JP 1997-542627	19970520

ANSWER 12 OF 27 SCISEARCH COPYRIGHT 2003 THOMSON ISI

AN 2003:354492 SCISEARCH

TI **Retroviral packaging** cells **encapsulated** in theracyte immunoisolation devices enable long-term in vivo gene delivery

SO FRONTIERS IN BIOSCIENCE, (MAY 2003) Vol. 8, pp. A94-A101.
Publisher: FRONTIERS IN BIOSCIENCE INC, C/O NORTH SHORE UNIV HOSPITAL, BIOMEDICAL RESEARCH CENTER, 350 COMMUNITY DR, MANHASSET, NY 11030 USA.
ISSN: 1093-9946.

AU Krupetsky A; Parveen Z; Marusich E; Goodrich A; Dornburg R (Reprint)

AB The method of delivering a therapeutic gene into a patient is still one of the major obstacles towards successful human gene therapy. Here we describe a novel gene delivery approach using TheraCyte immunoisolation devices. **Retroviral** vector producing cells, derived from the avian **retrovirus** spleen necrosis virus, SNV, were **encapsulated** in TheraCyte devices and tested for the release of **retroviral** vectors. In vitro experiments show that such devices release infectious **retroviral** vectors into the tissue culture medium for up to 4 months. When such devices were implanted subcutaneously in SCID mice, infectious virus was released into the blood stream. There, the vectors were transported to and infected tumors, which had been induced by subcutaneous injection of tissue culture cells. Thus, this novel concept of a continuous, long-term gene delivery may constitute an attractive approach for future in vivo human gene therapy.

L5 ANSWER 10 OF 27 MEDLINE
AN 2002015543 MEDLINE
TI In vivo perivascular implantation of **encapsulated packaging** cells for prolonged **retroviral** gene transfer.
SO JOURNAL OF MICROENCAPSULATION, (2001 Jul-Aug) 18 (4) 491-506. Journal code: 8500513. ISSN: 0265-2048.
AU Armeanu S; Haessler I; Saller R; Engelmann M G; Heinemann F; Krausz E; Stange J; Mitzner S; Salmons B; Gunzburg W H; Nikol S
AB Long-term benefits of coronary angioplasty remain limited by the treatment-induced renarrowing of arteries, termed restenosis. One of the mechanisms leading to restenosis is the proliferation of smooth muscle cells. Therefore, proliferating cells of the injured arterial wall, which can be selectively transduced by **retroviruses**, are potential targets for gene therapy strategies. A direct single-dose therapeutic application of **retroviral** vectors for inhibition of cell proliferation is normally limited by too low transduction efficiencies. **Encapsulated retrovirus**-producing cells release viral vectors from microcapsules, and may enhance the transduction efficiency by prolonged infection. Primary and immortal murine and porcine cells and murine **retrovirus**-producing cells were **encapsulated** in cellulose sulphate. Cell viability was monitored by analysing cell metabolism. Safety, stability, transfer efficiency and extent of restenosis using capsules were determined in a porcine restenosis model for local gene therapy using morphometry, histology, in situ beta-galactosidase assay and PCR. **Encapsulation** of cells did not impair cell viability. Capsules containing **retrovirus**-producing cells expressing the beta-galactosidase reporter gene were implanted into periarterial tissue or a pig model of restenosis. Three weeks following implantation, beta-galactosidase activity was detected in the pericapsular tissue with a transduction efficiency of approximately 1 in 500 cells. Adventitial implantation of vector-producing **encapsulated** cells for gene therapy may, therefore, facilitate successful targeting of proliferating vascular smooth muscle cells, and allow stable integration of therapeutic genes into surrounding cells. The **encapsulation** of vector-producing cells could represent a novel and feasible way to optimize local **retroviral** gene therapy.

L5 ANSWER 9 OF 27 MEDLINE
AN 2003192310 IN-PROCESS
TI **Encapsulation** of **packaging** cell line results in successful **retroviral**-mediated transfer of a suicide gene in vivo in an experimental model of glioblastoma.
SO EUROPEAN JOURNAL OF SURGICAL ONCOLOGY, (2003 May) 29 (4) 351-7. Journal code: 8504356. ISSN: 0748-7983.
AU Martinet O; Schreyer N; Reis E D; Joseph J-M
AB AIMS: **Retroviral**-mediated gene therapy has been proposed as a primary or adjuvant treatment for advanced cancer, because **retroviruses** selectively infect dividing cells. Efficacy of **retroviral**-mediated gene transfer, however, is limited in vivo. Although **packaging** cell lines can produce viral vectors continuously, such allo- or xenogeneic cells are normally rejected when used in vivo. **Encapsulation** using microporous membranes can protect the **packaging** cells from rejection. In this study, we used an **encapsulated** murine **packaging** cell line to test the effects of in situ delivery of a **retrovirus** bearing the herpes simplex virus thymidine kinase suicide gene in a rat model of orthotopic glioblastoma.MATERIALS AND METHODS: To test gene transfer in vitro, **encapsulated** murine psi2-VIK **packaging** cells were co-cultured with baby hamster kidney (BHK) cells, and the percentage of transfected BHK cells was determined. For in vivo experiments, orthotopic C6 glioblastomas were established in Wistar rats. Capsules containing psi2-VIK cells were stereotaxically implanted into these tumours and the animals were treated with ganciclovir (GCV). Tumours were harvested 14 days after initiation of GCV therapy for morphometric analysis.RESULTS: **Encapsulation** of psi2-VIK cells increased transfection rates of BHK target cells significantly in vitro compared to psi2-VIK conditioned medium (3x10(6) vs 2.3x10(4) cells; P<0.001). In vivo treatment with **encapsulated packaging** cells resulted in 3% to 5% of C6 tumour cells transduced and 45% of tumour volume replaced by necrosis after GCV (P<0.01 compared to controls).CONCLUSION: In this experimental model of glioblastoma, **encapsulation** of a xenogeneic **packaging** cell line increased half-life and transduction efficacy of **retrovirus** -mediated gene transfer and caused significant tumour necrosis.

ANSWER 1 OF 256 CAPLUS COPYRIGHT 2003 ACS

AN 1999:708935 CAPLUS

DN 131:332995

TI Construction of **retroviral producer** cells from adenoviral and **retroviral** vectors

SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2

IN Lin, Xinli; Tang, Jordan J. N.

AB The invention presents a method for making **retroviral producer** cells using adenoviral and **retroviral** vectors. The invention specifically presents the use of vectors based upon moloney murine leukemia virus (MLV) to deliver marker genes, and an adenovirus-based delivery system to deliver deliver MLV structural genes (gag, pol and env) to human cultured cells. The invention also presents a second viral vector system using the adenovirus-based delivery system to deliver deliver human immunodeficiency virus structural genes (gag, pol and env) to human cultured cells. The examples presented in the invention demonstrated the construction of these vectors as well as delivery and expression of the thymidine kinase gene and killing of tumors in mice following gancyclovir administration. The method described in this invention is based on the fact that to be converted to **producer** cells, human primary cells must acquire therapeutic or marker genes and structural genes. The former are delivered by a conventional MLV-based vector, while the later are delivered by the adenoviral vectors. The invention also discussed the potential use of the vectors and procedures presented in the invention for human gene therapy in which the new **producer** cells are **transplanted** into patients for continuous gene transfer.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9955894	A1	19991104	WO 1999-US9273	19990429
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2327444	AA	19991104	CA 1999-2327444	19990429
	AU 9937709	A1	19991116	AU 1999-37709	19990429
	AU 758155	B2	20030313		
	EP 1076714	A1	20010221	EP 1999-920141	19990429
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6303380	B1	20011016	US 1999-301846	19990429
	JP 2002512805	T2	20020508	JP 2000-546037	19990429

L9 ANSWER 2 OF 256 CAPLUS COPYRIGHT 2003 ACS
AN 1995:86722 CAPLUS
DN 122:23772
TI **Transplantation** of **retrovirus**-transduced canine keratinocytes expressing the .beta.-galactosidase gene
SO Gene Therapy (1994), 5(1), 317-22
CODEN: GETHEC; ISSN: 0969-7128
AU Stockschlaeder, Marcus A. R.; Schuening, Friedrich; Graham, Theodore C.; Storb, Rainer
AB We studied **transplantation** of **retrovirus** vector transduced canine keratinocytes to det. whether keratinocytes could persist and express the transferred gene after superficial **transplantation** to full-thickness wounds of dogs, a large random-bred model for gene transfer studies. Canine keratinocytes were transduced by co-cultivation with PA317 **retrovirus** **packaging** cells which produced helper-free amphotropic **retroviral** vectors (LZSN and LNPOZ) encoding the genes for .beta.-galactosidase (.beta.-gal) and neomycin phosphotransferase (neo). Efficient transfer and expression of the two genes could be demonstrated in confluent keratinocyte cultures for both vectors. When transduced keratinocytes were grown in organotypic cultures on a collagen matrix contg. autologous dermal fibroblasts at the air-liq. interface, the cultures showed well-organized and defined epidermal cell layers and several markers of terminal differentiation, including the presence of keratohyalin granules and a multilayered stratum corneum. To det. whether the transferred .beta.-gal gene was also expressed in vivo, we performed autologous **transplantation** of transduced keratinocytes onto full-thickness wounds of dogs. .beta.-Gal expressing keratinocytes could be demonstrated in situ in the regenerating epidermis 2 wk after **transplantation**. We conclude that keratinocytes can be efficiently transduced by **retroviral** vectors, that **retroviral** transduction does not interfere with proliferation or differentiation, and that transduced keratinocytes express the transferred gene after **transplantation** to full-thickness skin wounds of dogs. Keratinocytes thus seem to be good target cells for gene therapy.